

### REMARKS

Claims 1, 5-8, and 10-18 are pending in the application. Claims 1, 6, 8, and 10 have been amended. Claims 2-4 and 9 have been cancelled without prejudice. New claims 11-18 have been added. The specification has been amended to include reference characters that correspond to those in the drawings. Support for the amendments and new claims can be found in original claims 2-4 and 9 and in the specification at, e.g., page 5, lines 19-20; and page 8, lines 18-23. These amendments add no new matter.

#### Drawings

At page 2 of the Office Action, the drawings were objected to as including reference characters not mentioned in the description. The specification has been amended to include reference characters that correspond to those in the drawings. It is applicants' understanding that these amendments overcome the present objection.

#### 35 U.S.C. §112, Second Paragraph (Omission of Essential Steps)

At page 2 of the Office Action, claims 1-10 were rejected as being incomplete for omitting essential steps. Independent claim 1 has been amended to include a step of "transferring the expanded lymphocytes back into the patient." It is applicants' understanding that this amendment overcomes the rejection of claim 1 and the claims that depend therefrom.

#### 35 U.S.C. §112, First Paragraph (Enablement)

At pages 3-7 of the Office Action, claims 1-10 were rejected as failing to satisfy the enablement requirement.

Independent claim 1 has been amended to delete the reference to "preventing" cancer and to include a step of "transferring the expanded lymphocytes back into the patient." It is applicants' understanding that these amendments overcome, at least in part, the present rejection.

The currently claimed invention is based, at least in part, on the inventors' surprising discovery that sentinel lymph nodes isolated from cancer patients harbor lymphocytes showing

activity against tumor cells. In contrast to the sentinel lymph node-derived cells, lymphocytes isolated from peripheral blood or generically from the lymph system of the patients were unresponsive towards the tumor. Consistent with this discovery, the method of independent claim 1 includes steps of expanding in vitro lymphocytes obtained from sentinel lymph nodes from a human cancer patient and transferring the expanded lymphocytes back into the patient. Furthermore, the in vitro expansion step entails stimulation of the lymphocytes with IL-2, IFN- $\alpha$ , IL-12, an anti-IL-4 antibody, an anti-CD3 antibody, or an anti-CD28 antibody. The skilled artisan having read the present specification would have readily understand that any of these means of stimulating lymphocytes would be effective means to induce expansion of the sentinel lymph node-derived lymphocytes.

In view of the foregoing comments, applicants respectfully submit that the person of ordinary skill in the art, at the time the present application was filed, would have been able to practice the claimed methods without undue experimentation and with a reasonable expectation of success. As a result, applicants request that the Examiner withdraw the rejection.

35 U.S.C. §112, First Paragraph (Written Description)

At pages 7-10 of the Office Action, claim 10 was rejected as failing to satisfy the written description requirement.

Claim 10 has been amended to require that the kit contain: (i) a dye selected from the group consisting of patent blue dye, lymphazurine blue, and 99 Tc labeled albumin and (ii) a substance capable to stimulate proliferation of lymphocytes selected from the group consisting of IL-2, IFN- $\alpha$ , IL-12, an anti-IL-4 antibody, an anti-CD3 antibody, and an anti-CD28 antibody. It is applicants' understanding that this amendment overcomes the rejection under this heading.

35 U.S.C. §102 (Anticipation)

(i) Chin et al.

At page 10 of the Office Action, claims 1, 5, 6, and 9 were rejected under 35 U.S.C. §102(b) as anticipated by Chin et al. (2002) *Annals of Surgical Oncology* 9(1):94-103.

Independent claim 1 has been amended to incorporate the limitations of original claims 2-4, which claims were not rejected under this heading. It is applicants' understanding that this amendment overcomes the present rejection.

(ii) Harada et al. and (iii) Okamoto et al.

At pages 10-11 of the Office Action, claims 1, 2, 4-6, and 9 were rejected under 35 U.S.C. §102(b) as anticipated by Harada et al. (1996) *Immunology* 87:447-53 ("Harada") as evidenced by National Cancer Institute. In a similar rejection at pages 11-12 of the Office Action, claims 1, 2, and 4-9 were rejected as anticipated by Okamoto et al. (1995) *Cancer Immunol. And Immunother.* 40:173-81 ("Okamoto") as evidenced by National Cancer Institute.

Independent claim 1 is directed to the treatment of a human cancer patient. In contrast, Harada and Okamoto each describe experimentation performed in mouse tumor models. Because Harada and Okamoto do not describe the treatment of a human cancer patient, each of the references fails to anticipate claim 1 for this reason alone.

In addition to the foregoing, Harada and Okamoto do not describe the isolation and expansion of lymphocytes obtained from "sentinel lymph nodes," as is required by claim 1. As detailed in the present application, "sentinel lymph nodes" are defined as the first lymph nodes in the lymphatic system that receive lymphatic drainage from a primary tumor area (see specification at page 5, lines 10-11; emphasis added). In contrast, the mice used in each of Harada and Okamoto were inoculated subcutaneously in the abdomen with tumor cells lines. As a result of the use of inoculated tumor cell lines, these mice did not have any primary tumors. Due to the lack of primary tumors in the mouse model systems of Harada and Okamoto, it

necessarily follows that the lymphocytes derived from these mice could not have been derived from sentinel lymph nodes, as is required by the claims.

In view of the foregoing remarks, applicants respectfully submit that each of Harada and Okamoto do not anticipate independent claim 1 or the claims that depend therefrom. Applicants respectfully request that the Examiner withdraw the rejection.

(iv) US20030228635

At pages 12-13 of the Office Action, claim 10 was rejected under 35 U.S.C. §102(c) as anticipated by US20030228635.

Claim 10 has been amended to require that the kit contain: (i) a dye selected from the group consisting of patent blue dye, lymphazurine blue, and 99 Tc labeled albumin and (ii) a substance capable to stimulate proliferation of lymphocytes selected from the group consisting of IL-2, IFN- $\alpha$ , IL-12, an anti-IL-4 antibody, an anti-CD3 antibody, and an anti-CD28 antibody. US20030228635 fails to disclose a kit containing the combination of a dye and a substance capable to stimulate proliferation of lymphocytes as recited in claim 10. As a result, applicants respectfully request that the Examiner withdraw the rejection.

#### Obviousness-Type Double Patenting

At pages 13-16 of the Office Action, claims 1, 2, and 4-9 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over (i) claims 90-109 of copending application serial number 12/158,683; (ii) claims 90-109 of copending application serial number 12/158,680; and (iii) claims 1-33 of copending application serial number 12/147,752. The allegedly conflicting claims of application serial numbers 12/158,683, 12/158,680, and 12/147,752 have not been patented. For this reason, the present rejections are a provisional obviousness-type double patenting rejections. In view of the remarks presented herein, it is applicants' understanding that the provisional obviousness-type double patenting rejections are the only rejections remaining in the present application. Accordingly, the double patenting rejections should be withdrawn to permit the present

application to issue as a patent. See MPEP § 804.I.B. Because none of application serial numbers 12/158,683, 12/158,680, and 12/147,752 has issued as a patent, no terminal disclaimer is required for the present application. Applicants respectfully request that the Examiner withdraw the rejection.

### CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Please apply charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 20084-0002US1.

Respectfully submitted,

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